Correspondence

The Editors will be pleased to receive and consider for publication correspondence containing information of interest to physicians or commenting on issues of the day. Letters ordinarily should not exceed 600 words and must be typewritten, double-spaced, and submitted in duplicate (the original typescript and one copy). Authors will be given the opportunity to review the editing of their correspondence before publication.

Niacin Benefits

To THE EDITOR: The editorial by Malloy and colleagues in the October 1991 issue[1] graphically outlines the side effects of niacin therapy. It should dampen enthusiasm for self-medication.

What, however, is the risk/benefit ratio for niacin? Clearly, we cannot simply tell patients, "It is the only drug so far associated with increased survival in an intervention trial," as stated in the editorial.

Few patients will opt for niacin therapy if they are given a candid summary of the trial, that is, cholesterol reduction resulted in increased mortality (21.2% vs 20.9%) during niacin therapy.[2]

After the five-year trial, serum cholesterol levels *rose* to pretreatment levels when niacin was discontinued. Three years later, the treated group began to show reduced mortality (24.4% vs 25.4%), and this difference continued to widen at ten years' follow-up (52% vs 58.2%).[3]

Thus, we have an inverse relationship between cholesterol and mortality: the niacin-induced drop in cholesterol levels was associated with higher immediate mortality, and a posttherapy rise in cholesterol was followed by lower mortality.

There is no evidence that *continued* niacin therapy would result in this same improved survival, and the meta-analysis by Muldoon and associates suggests that cholesterol reduction may often result in a discouraging increase in overall mortality.[4]

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Drs Malloy and Kane Respond

To THE EDITOR: Dr Bassler's letter raises the question of the risk and benefit of hypolipidemic therapy in the context of treatment with niacin. Although he alludes to increased mortality among those treated with niacin during the Coronary Drug Project trial, the difference (21.2% vs 20.9%) in mortality is so small as to be biologically meaningless. The difference in mortality in the decade following the study was, however, impressive (and statistically significant). That the serum cholesterol levels rose when niacin was discontinued was predictable. The most reasonable explanation for the diminished mortality in the years following the trial among those who took niacin is based on our current understanding of the natural history of coronary artery disease in which most lesions tend to increase gradually in size toward the initiation of clinical events. Inhibited progression or regression of lesions during treatment with niacin could thus be expected to result in postponement of some lethal events later in life.

A number of critics of lipid-lowering therapy have based their analyses on single drug trials that achieved marginal effects on lipoproteins. Many have restricted their analyses to the relatively short trial periods. Based on the assumption, now known to be erroneous, that lesions would not regress but that progression might be inhibited, nearly all such trials were conducted on men in age groups in which new coronary events are uncommon. It is clear that limiting the analysis of benefit to the relatively small differences observed between control and treated groups in these trials greatly underestimates the benefit that would be expected if the differences in the rate of progression or regression were projected out to the later decades of life where clinical coronary events are numerous. Thus, this "delta Y tangent" effect should be the appropriate analysis of the effectiveness of lipid-lowering therapy.

Nearly every epidemiologic survey has identified a positive relationship between levels of atherogenic lipoproteins in blood and the risk of coronary artery disease. Three recently reported angiographic trials, all of which included niacin in combined drug regimens, demonstrated significant regression of coronary placques during aggressive therapy for hyperlipidemia.[1-3] These studies strongly support the lipid hypothesis that a reduction in levels of atherogenic lipoproteins in plasma can prevent or delay the emergence of clinical coronary artery disease. Therefore, treatment designed to achieve ideal levels of atherogenic lipoproteins has a strong mechanistic basis and is a rational intervention pending the availability of data from long-term studies.

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